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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/402,282	04/24/2000	RICHARD SETON TEDDER	6508.US.01	5742

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EXAMINER	
PENG, BO	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/402,282	TEDDER ET AL.	
	Examiner	Art Unit	
	Bo Peng	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-10,12-18,20-23,26,28-31,38,40,42,43 and 59-97* is/are pending in the application.

4a) Of the above claim(s) *8,9,17,18,20-23,26,28-31,38,40,42,43 and 81-95* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10,12-16,59-80,96 and 97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to the amendment filed 17 November 2006. Claims 7, 11, 19, 24, 25, 27, 32-37, 39, 41 and 44-58 are cancelled. New Claims 96 and 97 are added.

2. Accordingly, Claims 1-6, 8-10, 12-18, 20-23, 26, 28-31, 38, 40, 42, 43 and 59-97 are pending. Claims 8, 9, 17, 18, 20-23, 26, 28-31, 38, 40, 42, 43 and 81-95 are withdrawn as non-elected. Claims 1-6, 10, 12-16, 59-80, 96 and 97 are considered in this Office action. **This is a Non-final**.

3. The objection to Claim 10 **is withdrawn** in view of the Applicant's amendment.

35 USC § 112, second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The rejection of Claims 1, 4, 6, 11 and 60-70 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, **is withdrawn** in view of Applicant's argument and the amendment to the claims.

35 USC § 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his

invention.

7. The rejection of Claims 13, 14 and 15 under 35 U.S.C. 112, first paragraph for failing to comply with the rule of biological material **is withdrawn** in view of the statement by the Attorney that the specific strains of hybridoma cells as recited in Claims 13, 14 and 15 will be irrevocably and without restriction or condition released to the public upon the issuance of a U.S. patent (Remarks, p. 16 and 17).

8. The rejection of Claims 1-6, 10, 12-16 and 59-80 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement **is maintained**, and is now extended to new Claims 96 and 97.

9. Applicant argues that the instant claims fully complied with the Federal Circuit's requirements as articulated in Noelle because the specification describes HBsAg and the major neutralizing epitope of HBV, termed the 'a' determinant, and the specification also describes that the claimed monoclonal antibody has the capability of binding to both the wild-type and to at least two mutant forms of HBsAg. Additionally, the specification describes the isolation and characterization of several specific monoclonal antibodies that are capable of binding to the wild-type and to at least two mutant forms of HBsAg, namely, the monoclonal antibodies produced by the P2D3, M3A10, and M4F5 clones.

10. Applicant's argument is considered, but found not persuasive for following reasons: First of all, according to "Guidelines for Examination of Patent Application under 35 U.S.C. 112, first paragraph, 'Written Description' Requirement" 66 F. R. 1099, 1150: "The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature that is not described in the specification and is not conventional in the art or known to

one of skill in the art" (Jan 5, 2001, left column, first paragraph). The instant claims lack written description because the essential features of "the mutant forms of HBsAg" are not described. Although a few HBsAg mutants, such as Gly145Arg, were disclosed, little is known about other HBsAg mutants in the prior art at the time the application was filed. Since the structural features of "the mutant forms of HBsAg" are not described, the claimed monoclonal antibodies that "are capable of binding to wild-type HBsAg and to at least two mutant forms of HBsAg" does not have sufficient characteristic for written description.

11. Secondly, since there are no specific structural limitations to the mutant forms of HBsAg described in the instant claims, the mutant form of HBsAg is not defined and could be any amino acid substitutions in HBsAg. Thus, the claims encompass a genus of monoclonal antibodies that "are capable of binding to wild-type HBsAg and to at least two mutant forms of HBsAg". The MPEP states that written description for a genus can be achieved by a representative number of species within a broad genus. Here, while having written description of a few specific antibodies that are able to bind two or three strains of NP and MAM HBsAg variants identified in the specification tables and/or examples, the specification has not disclosed sufficient variety of monoclonal antibodies that "are capable of binding to wild-type HBsAg and to at least two mutant forms of HBsAg". Although the claims recite functional characteristics that "are capable of binding to wild-type HBsAg and to at least two mutant forms of HBsAg", there is no disclosure of a correlation between functional characteristics of claimed antibodies and structure of "mutant forms of HBsAg" beyond those disclosed in the examples in the specification.

12. Consequently, while the skilled artisan would reasonably conclude Applicant was in possession of a few monoclonal antibodies to HBsAg, there is no indication that Applicant was

in possession of a genus of monoclonal antibodies that is capable of binding specifically to wild-type HBsAg and to any two known or unknown HBsAg variants as broadly claimed.

13. Following are new grounds of rejections:

Claim Rejections - 35 USC § 102

14. The following is a quotation from the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 1-6, 12, 59-75 and 96 are rejected under 35 U.S.C. 102(b) as being anticipated by Mangold CM et al. (1995, Virology, Vol. 211, p.535-543).

16. Claims 1-6, 12, 59-75 and 96 are directed to a monoclonal antibody that is capable of binding specifically to wild-type HBsAg and to at least two mutant forms of HBsAg, wherein at least one of said two mutant forms of HBsAg has at least one amino acid substitution relative to wild type HBsAg, wherein at least one of said two mutant forms of HBsAg has the sequence of HBsAg present in an HBV escape mutant, wherein at least one of said two mutant forms of HBsAg has at least one amino acid substitution in the "a" determinant, wherein an amino acid substitution results from a point mutation, wherein at least one of said two mutant forms of HBsAg has an amino acid substitution within the sequence comprising amino acids 133 to 145 of

HBsAg; A monoclonal antibody that binds specifically to wild-type HBsAg and to at least two mutant forms of HBsAg.

17. Mangold teaches that monoclonal antibody H53 is capable of binding specifically to wild-type HBsAg and at least two mutant forms of HBsAg, such as HBsAg Cys139Ala and HBsAg Cys147Ala, (Table 2). Mangold also teaches that monoclonal antibody H166 is capable of binding specifically to wild-type HBsAg and at least two mutant forms of HBsAg, such as HBsAg Cys137/138/139Ala, HBsAg Cys137Ala, and Cys139Ala (Table 2). Mangold teaches that those HBsAg variants strongly reduced their antigencity compare to the wt HBsAg, and lost their reactivity to some other mAbs against wt HBsAg, such as H5, H10 and H35 (Table 2 and right column p. 541). Therefore, those HBsAg variants are capable of escaping from the neutralizing mAbs H5, H10 and H35.

18. Since monoclonal antibodies H53 and H166 meet the structural and functional limitations of Claims 1-6, 12, 59-75 and 96, the instant claims are anticipated by Mangold.

Claim Rejections - 35 USC § 102/103

19. Claims 1-6, 12, 59-75 and 96 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Waters et al. (WO 94/21812).

20. Waters et al. disclose monoclonal antibodies SMH HBs 145/G/R/I and SMH HBs 145/G/R/II that bind to HBV variants containing a glycine to arginine substitution mutation at position 145 within the "a" determinant region of HBsAg. Waters also teaches that monoclonal antibodies SMH HBs 145/G/R/I and SMH HBs 145/G/R/II can bind both variant HBsAg and wild type HBsAg (line 33, p. 6 to line 5, p. 7 and Paragraph 4, p. 8).

21. Given the fact that there is no structural limitations to "mutant forms of HBsAg" in the instant claims, and given the knowledge that monoclonal antibodies SMH HBs 145/G/R/I and SMH HBs 145/G/R/II can cross-react with both variant HBsAg and wild type HBsAg, as disclosed by Waters et al., monoclonal antibodies SMH HBs 145/G/R/I and SMH HBs 145/G/R/II must inherently react with other "mutant forms of HBsAg", which contain epitopes that are structurally close to the epitopes to which SMH HBs 145/G/R/I and SMH HBs 145/G/R/II bind. Therefore, monoclonal antibodies SMH HBs 145/G/R/I and SMH HBs 145/G/R/II meet the limitations of the claims directed to nucleic acids.

Remarks

22. Claims 13-15 are free of the prior art and allowable.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on M-F, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, Ph. D. can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

BP
Bo Peng, Ph.D.
February 14, 2007

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SUPERVISORY PATENT EXAMINER
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